REMARKS

The First Obviousness-type Double Patenting Rejection

Claims 1 and 30 are rejected as allegedly unpatentable under obviousness type double patenting over claim 51 of co-pending US 10/857,877.

The claims of the present application are directed to a method for "MR imaging for visualization of intravascular thrombi" where certain complexes are administered as contrast media "to a subject who is to undergo MR imaging for determination of the presence of intravascular thrombi" and where the method includes "visualizing intravascular thrombi in said subject with an MR imaging apparatus."

The claimed method is not obvious over the claims of US '877, which are directed a method of "conducting MRI imaging, and visualizing plaque, infarcted tissue, or necrotic tissue in which contrast agent is uptaken, or independently simultaneously visualizing necroses and tumors in which contrast agent is uptaken." (Emphasis added.) See the last part of independent claim 51, on page 11 of the preliminary amendment of 'US '877.

The only reason provided for the rejection in the Office Action dated October 6, 2006, is that both the methods of the present application and of the reference's claims use the same complexes.

However, merely establishing that the complexes used in the methods of the reference and of the present claims are the same is inadequate to establish obviousness-type double patenting. The methods of the present claims are not taught or suggested by the method claims of the reference. Nothing in the claims of US '877 directs one of ordinary skill in the art to administer the complexes claimed therein "to a subject who is to undergo MR imaging for determination of the presence of intravascular thrombi" and nothing therein teaches or suggests that the complexes are suitable for "visualizing intravascular thrombi."

The Office Action dated May 19, 2006, provides more thorough allegations, where it is alleged that the claims of the reference application and of the present application teach methods where the contrast agents are "used for the same type of imaging," and thus, "the applications contain overlapping subject matter." See end of second paragraph of page 3 of Office Action.

Imaging "intravascular thrombi" does not overlap the imaging of "plaque, infarcted tissue, or necrotic tissue" or of "necroses and tumors." While very broadly one can say that both

visualizations are done with a contrast agent using MRI, such generalization merely defines a universe of imaging methods with many non-overlapping species. Just because two inventions are within the same universe of technology very broadly speaking, it does not follow that every invention within such universe is obvious in view of other inventions therein. However, such is the basis of the rejection here, which is improper.

One of ordinary skill in the art facing a teaching that a contrast agent, for example, accumulates in plaque, infarcted tissue, or necrotic tissue or necroses and tumors, and makes their visualization possible using MRI, would not be motivated to use the same contrast agent for intravascular thrombi to making its MRI visualization possible. Nor would there be a reasonable expectation of success of such visualization.

For example, the mechanism of contrast agent uptake is a variable that is expected to be different among these various tissues, structures, etc., based on the completely different histopathological composition of these various tissues, structures, etc. One of ordinary skill in the art would expect that these variations in tissues, structures, etc., and the various mechanisms of uptake of contrast agent to influence whether such tissues, structures, etc., can be visualized when subjected to a specific contrast agent. The targets of the reference's claims do not render obvious the target of the present claims.

Moreover, no factual basis has been provided in the rejection that would support that one of ordinary skill in the art would expect that a contrast agent useful for the visualization of the reference's various tissues, structures, etc., would also be useful for the visualization of intravascular thrombi.

At most the allegations may be adequate to support an allegation that it may be obvious to try, which is not admitted, to visualize various tissues and/or structures, e.g., bone tissues, vascular tissues, nerve tissues, liver tissue, etc., using the contrast agent of the reference with MRI and see for which tissues and/or structures the imaging provides useful MR images. However, obvious to try is not the test for obviousness-type double patenting. See *Abbott Laboratories v. Andrx Pharmaceuticals Inc.*, 79 USPQ2d 1321 (CA FC 2006). Something in the prior art must teach or suggest the modification to one of ordinary skill in the art to achieve the claimed invention for such to be obvious, or for such to be unpatentable under obviousness-type double patenting. That is lacking in the rejection made against the present claims.

For all the foregoing reasons, the claims of the present application are not obvious from the claims of US '877.

The Second Obviousness-type Double Patenting Rejection

Claims 1-29 and 45-49 are rejected as allegedly unpatentable under obviousness type double patenting over claims 1-35 of US 6,818,203.

Claims 1-35 of US '203 are directed to a method of MRI imaging where "plaque in which contrast agent is uptaken," or "necroses and tumors in which contrast agent is uptaken" are visualized.

The allegation in this rejection too, as in the rejection discussed above, relies on the same complexes being used in the various methods. However, nothing in the reference's claims directs one of ordinary skill in the art to administer the complexes claimed therein "to a subject who is to undergo MR imaging for determination of the presence of intravascular thrombi" and nothing therein teaches or suggests that the complexes are suitable for "visualizing intravascular thrombi."

Thus, the arguments from above, as they apply to this second rejection too, are incorporated herein also.

The Sections 101 and 112 Rejections

Applicants respectfully disagree that the claims did not set froth any steps involved in the process. The recitation "using, as contrast media for visualization" clearly conveys to one of ordinary skill in the art what steps ate to be taken in the claimed method. Nevertheless, to advance prosecution, the claims have been amended, rendering moot the rejections.

The Sections 103 Rejections

The two 103 rejections refer to two applications by Platzek et al. that are cited in the description of the present invention. Both disclose compounds that can be used in the method of the instant invention. Both references disclose certain applications of said compounds, amongst others broadly for imaging of vascular disease. Both references fail to disclose a method wherein said compounds are used for imaging of vascular thrombi, which is admitted by the Office

Action. The Office Action alleges that, since vascular disease and thrombus are pathologies of the same tissue, it would have been obvious for the skilled person that said compounds will also work for imaging thrombi.

Both references, when referring to the use of said compounds for imaging vascular disease, point to the blood pool characteristics of these compounds that make such use possible.

WO99/01161's US equivalent 6,641,797's column 19, lines 12-26, teaches that

> The compounds according to the invention are also extremely well suited for detecting and localizing vascular diseases, since they are dispersed exclusively in the latter in the administration in the intravascular space. The compounds according to the invention make it possible, with the help of nuclear spin tomography, to distinguish between tissue that is well supplied with blood and tissue that is poorly supplied with blood and thus to diagnose an ischemia. Because of its anemia, infarcted tissue can also be distinguished from surrounding healthy or ischemic tissue, when the contrast media according to the invention are used. This is of special importance if the point is, e.g., to distinguish a myocardial infarction from an ischemia.

WO97/26017's US equivalent 6,916,461's column 2, lines 47-59, recites a paragraph, that is near identical to the paragraph cited above.

Both references also explicitly teach the use of the compounds as "blood-pool agents." See US '979's first sentence in the specification, and US '017's abstract.

In sum, the references teach that the compounds of the invention therein when imaging vascular disease make it possible to distinguish tissue that is well-supplied with blood from tissue that is poorly supplied with blood.

A skilled person would not have expected that such a compound would also work for positively imaging a thrombus. For imaging a thrombus the image can not be based on a difference in blood supply which may be imaged by a blood pool agent, but needs to be based on direct accumulation of the diagnostic compound at the structure to be imaged (here the thrombus).

From the disclosure of the cited references regarding vascular disease, one of ordinary skill in the art would be motivated to use the compounds for distinguishing well-supplied tissue from poorly-supplied tissue, which would have been expected from the disclosure to lead to a

lack of signal at a site where blood flow is barred. Based on the lack of signal, one of ordinary skill in the art would not know what may be the cause of the barred blood flow. Additionally, one of ordinary skill in the art would not expect to get an image particularly of the structure that bars the blood flow. Consequently, the skilled person would not consider the compounds disclosed in the cited references when looking for a compound that is suitable for use in a method of generating an image of a vascular thrombus.

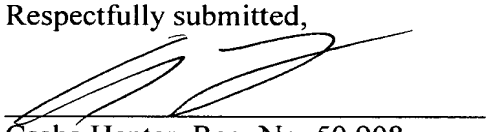
Reconsideration is respectfully requested.

Other Issues

In claim 30, G is defined as being selected from k) or l). In the last reply, inadvertently the formula for k) was left out from the claim. It was never deleted formally, i.e., no cross-through, but merely absent. This was an inadvertent error. It was never intended to be omitted or otherwise deleted from the claim. The formula for k) is inserted back into claim 30. No markup is provided for such reintroduction of formula k), i.e., underlining, since it was never formally deleted from claim 30.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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